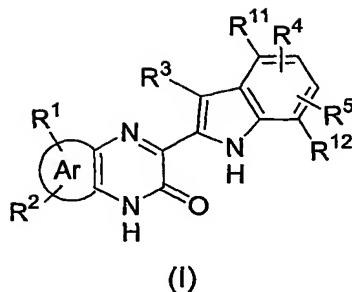


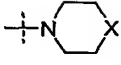
What is claimed is:

1. A compound of Formula I



wherein

 represents a 6 membered aromatic ring containing 0, 1 or 2 N atoms;

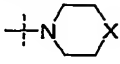
R^1 and R^2 are each independently selected from H, halo, CF_3 , $C(O)R^9$, ,
(C_1 - C_6)alkyl optionally substituted with up to two substituents selected from
OH, (C_1 - C_3)alkoxy, F, and phenyl,

(C_1 - C_6)alkoxy optionally substituted with one or two substituents each

independently selected from  and

$N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted
up to two times with (C_1 - C_3)alkoxy,

$NH(C_1-C_3)alkyl$ where said alkyl is optionally substituted with up to two
substituents each selected independently from OH, F, (C_1 - C_3)alkoxy,

$N[(C_1-C_3)alkyl]_2$, $NH(C_1-C_3)alkyl$, phenyl, pyrrolidinyl, and ,

$N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted
with up to two substituents each selected independently from OH, F,
phenyl, and (C_1 - C_3)alkoxy, said alkoxy being optionally

substituted with ,

pyrrolidinyl optionally substituted up to two times with $N[(C_1-C_3)alkyl]_2$,

phenyl optionally substituted with up to two substituents each selected
independently from (C_1 - C_3)alkyl, (C_1 - C_3)alkoxy, halo, CF_3 , and CN,

with the proviso that when  contains 1 or 2 N atoms, R^1 and R^2 must each be
H,

and, R^1 and R^2 together with the adjacent C atoms to which they are attached
form a ring selected from benzo, dioxolo and imidazo,

said imidazo being optionally substituted up to two times with
(C₁-C₃)alkyl,

with the proviso that R¹ and R² together with the adjacent C atoms to

which they are attached form a ring only when  contains no N atoms;

R³ is selected from H, (C₁-C₄)alkyl, OH, NO₂, NH₂, NH(C₁-C₄)alkyl, NHC(O)(C₁-C₄)alkyl

and NHC(O)phenyl, said phenyl being optionally substituted with up to two
substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo,
CF₃, and CN;

R⁴ is selected from H, OH, halo, CN, C(O)R⁶, S(O)₂R⁷, OSi[(C₁-C₄)alkyl]₃, tetrazolyl,
thienyl, pyrrolyl, pyrimidinyl, oxazolyl, furanyl,

(C₁-C₆)alkyl, (C₂-C₆)alkenyl or (C₂-C₆)alkynyl, each optionally substituted with
OH, F, OC(O)NHphenyl, NHC(O)(C₁-C₃)alkyl, C(O)NH₂,

C(O)NH(C₁-C₃)alkyl, C(O)N[(C₁-C₃)alkyl]₂, ,

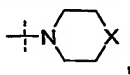
(C₁-C₃)alkoxy optionally substituted up to two times with (C₁-C₃)alkoxy,

NHC(O)NH(C₁-C₃)alkyl where said alkyl is optionally substituted

with up to two substituents independently selected from OH,

(C₁-C₃)alkoxy, F and phenyl,

NHC(O)NHphenyl where said phenyl is optionally substituted with up to
two substituents independently selected from (C₁-C₃)alkyl,

(C₁-C₃)alkoxy, halo, CF₃, CN, and ,

NHC(O)N[(C₁-C₃)alkyl]₂ where each alkyl is independently

optionally substituted up to two times with (C₁-C₃)alkoxy,

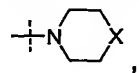
NH-phenyl, said phenyl being optionally substituted with up to two
substituents independently selected from (C₁-C₃)alkyl,

(C₁-C₃)alkoxy, halo, CN, and ,

N[(C₁-C₃)alkyl]₂ where each alkyl is independently

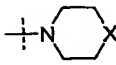
optionally substituted up to two times with (C₁-C₃)alkoxy,

phenyl optionally substituted with up to two substituents independently
selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CN, CF₃, and



pyrrolidinyl optionally substituted up to two times with N[(C₁-C₃)alkyl]₂,

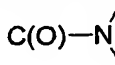
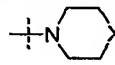
(C₁-C₆)alkoxy optionally substituted with up to two substituents independently

selected from (C₁-C₃)alkoxy, pyrrolidinyl, ,
and N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally
substituted with up to two substituents independently selected from
OH, F, (C₁-C₃)alkoxy and phenyl,

N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally
substituted with up to two substituents independently selected from OH,
(C₁-C₃)alkyl, F, (C₁-C₃)alkoxy, and phenyl,

oxadiazolyl optionally substituted up to two times with (C₁-C₃)alkyl,

phenyl optionally substituted with up to two substituents independently selected

from (C₁-C₃)alkoxy, CN, (C₁-C₃)alkyl, halo, , ,
C(O)(C₁-C₃)alkyl optionally substituted with up to two substituents
independently selected from (C₁-C₃)alkoxy, OH, (C₁-C₃)alkoxy,
F, and phenyl, and

C(O)N[(C₁-C₃)alkyl]₂ where each of said alkyl groups are independently
optionally substituted up to two times with (C₁-C₃)alkoxy,

pyridyl optionally substituted with up to two substituents independently selected
from (C₁-C₃)alkyl,

C(O)N[(C₁-C₃)alkyl]₂ where each of said alkyl groups are independently optionally
substituted up to two times with (C₁-C₃)alkoxy, and

O-pyridyl optionally substituted with up to two substituents independently selected
from CF₃, halo, and (C₁-C₃)alkyl;

R⁵ is selected from H, halo, CN, (C₁-C₆)alkoxy, and (C₁-C₆)alkyl;

R⁶ is selected from OH, NHR¹⁰, O-(C₃-C₆)cycloalkyl, (C₁-C₃)alkoxy, O-(C₂-C₆)alkenyl,
O-(C₃-C₆)alkynyl,

(C₁-C₆)alkyl optionally substituted with up to two substituents independently
selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally
substituted with up to two substituents independently selected from OH,
CN, N[(C₁-C₄)alkyl]₂, (C₁-C₃)alkoxy, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl,
phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl, and pyridyl,

N[(C₁-C₃)alkyl]R⁸ where [(C₁-C₃)alkyl] is optionally substituted up to two times with
(C₁-C₃)alkoxy,

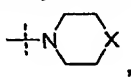
N[(C₃-C₆)cycloalkyl](C₁-C₃)alkyl where said alkyl is substituted with up to two
substituents independently selected from (C₁-C₃)alkoxy, OH, CN,

N[(C₁-C₄)alkyl]₂, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₅-C₆)cycloalkyl, and pyridyl,

pyrrolidinyl optionally substituted with up to two substituents independently selected from NH₂, NH(C₁-C₃)alkyl, N[(C₁-C₄)alkyl]₂, C(O)NH₂, NHC(O)(C₁-C₃)alkyl, NHS(O)₂(C₁-C₃)alkyl, pyridyl, N[(C₁-C₃)alkyl]C(O)NH(C₁-C₃)alkyl, N[(C₁-C₃)alkyl]C(O)(C₁-C₃)alkyl, and (C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from N[(C₁-C₄)alkyl]₂, (C₁-C₃)alkoxy, and pyrrolidinyl,

morpholinyl optionally substituted up to two times with (C₁-C₃)alkyl, thiomorpholinyl optionally substituted up to two times with (C₁-C₃)alkyl, piperazinyl optionally substituted with up to two substituents independently

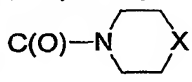
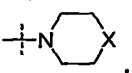
selected from pyrazinyl, C(O)NH₂, C(O)NH-phenyl, C(O)-furyl, C(O)(C₁-C₃)alkyl, C(O)NH(C₁-C₃)alkyl, C(O)N[(C₁-C₃)alkyl]R⁸,

S(O)₂(C₁-C₃)alkyl, S(O)₂-phenyl, ,

pyridyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, CN and CF₃,

phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, CN, halo, CF₃, and (C₁-C₃)alkoxy,

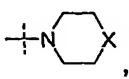
(C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from OH, F, phenyl, (C₁-C₃)alkoxy,

N[(C₁-C₃)alkyl]₂, pyrrolidinyl, C(O)-pyrrolidinyl, , , and

pyridyl optionally substituted up to two times with (C₁-C₃)alkoxy,

and

piperidinyl optionally substituted with up to two substituents independently selected from phenyl, pyridyl, pyrrolidinyl and oxo-dihydrobenzimidazolyl;

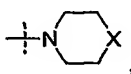
R⁷ is selected from NH₂, pyrrolidinyl, ,


NH(C₁-C₃)alkyl said alkyl being optionally substituted up to two times with (C₁-C₃)alkoxy,

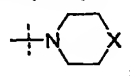
NH-phenyl said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, CN, (C₁-C₄)alkoxy, halo and CF₃,

N[(C₁-C₃)alkyl]₂ wherein each alkyl is independently optionally substituted up to

two times with (C₁-C₄)alkoxy, and
 phenyl optionally substituted with up to two substituents independently selected
 from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃ and CN;
 R⁸ is selected from (C₁-C₃)alkoxy, pyridyl, piperidiny, pyranyl and
 phenyl, where each ring moiety is optionally substituted with up to two
 substituents independently selected from (C₁-C₃)alkoxy, and
 (C₁-C₃)alkyl;

R⁹ is selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, OH, ,
 phenyl optionally substituted with (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN,
 N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally
 substituted with OH, CN, N[(C₁-C₄)alkyl]₂, (C₁-C₄)alkoxy, S(O)₂-phenyl,
 S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl,
 and pyridyl, and
 pyrrolidiny optionally substituted with N[(C₁-C₃)alkyl]₂,

and, only when  contains no N atoms, R⁹ is also selected from pyridyl,
 thienyl, and NHR¹⁰;

R¹⁰ is selected from H, indolyl,
 (C₁-C₄)alkyl optionally substituted with up to two substituents independently
 selected from OH, F, phenyl, (C₁-C₄)alkoxy, NHC(O)(C₁-C₃)alkyl,
 S-(C₁-C₃)alkyl, benzimidazolyl, indolyl, thienyl, pyrazolyl, ,
 N[(C₁-C₄)alkyl]₂ where each alkyl is independently optionally
 substituted with up to two substituents independently selected from
 OH, (C₁-C₃)alkoxy, F, and phenyl,
 phenyl optionally substituted with up to two substituents independently
 selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, CN, halo,
 CF₃, S(O)₂(C₁-C₃)alkyl, S(O)₂phenyl, and S(O)₂NH₂,
 pyridyl optionally substituted up to two times with CF₃,
 imidazolyl optionally substituted up to two times with (C₁-C₃)alkyl,
 furyl optionally substituted up to two times with (C₁-C₄)alkyl, and
 pyrrolidiny optionally substituted with up to two substituents independently
 selected from (C₁-C₄)alkoxy, (O), and
 (C₁-C₄)alkyl optionally substituted with up to two substituents
 independently selected from OH, (C₁-C₃)alkoxy, F,

and phenyl,

S(O)₂-phenyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (C₁-C₃)alkyl, halo, and CN,

pyrazolyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl, and

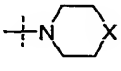
phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (C₁-C₄)alkyl, halo, CF₃, and CN,

benzothiazolyl optionally substituted up to two times with (C₁-C₄)alkyl,

thiazolyl, optionally substituted up to two times with (C₁-C₄)alkyl,

thiadiazolyl, optionally substituted with up to two substituents independently selected from CF₃, (C₃-C₆)cycloalkyl, and (C₁-C₆)alkyl,

phenyl optionally substituted with up to two substituents independently selected

from CN, halo, CF₃, N[(C₁-C₄)alkyl]₂, indolyl, ,

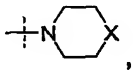
O-pyridyl optionally substituted with C(O)NH(C₁-C₄)alkyl,

(C₁-C₄)alkyl optionally substituted with up to two substituents

independently selected from pyridyl, , OH,

(C₁-C₃)alkoxy, F, and phenyl, and

(C₁-C₄)alkoxy optionally substituted with N[(C₁-C₄)alkyl]₂ where one alkyl group is optionally substituted with phenyl, or

(C₁-C₄)alkoxy optionally substituted with ,

pyridyl optionally substituted with phenoxy where said phenoxy is optionally

substituted with up to two substituents independently selected

from (C₁-C₄)alkyl and (C₁-C₄)alkoxy, and

indazolyl optionally substituted up to two times with (C₁-C₄)alkyl;

R¹¹ and R¹² are each selected independently from H, F and Cl with the proviso that when one of R¹¹ and R¹² is F or Cl, the other must be H;

X is selected from O, S, CH₂, and NH, and

when X is NH, the H on NH is optionally replaced with pyridyl, pyrazinyl, phenyl,

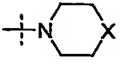
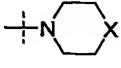
or (C₁-C₄)alkyl optionally substituted with up to two substituents



independently selected from OH, (C₁-C₃)alkoxy, N[(C₁-C₃)alkyl]₂,

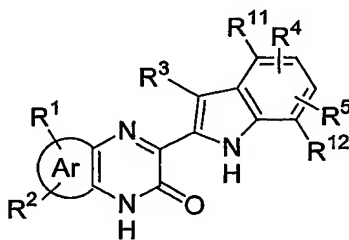
C(O)-pyrrolidinyl, N[(C₁-C₄)alkyl]₂, and phenyl said phenyl being

optionally substituted with up to two substituents

independently selected from CN and (C₁-C₃)alkoxy,

and when X is O, S, or CH₂, the  moiety is optionally substituted by replacing any H atom in the  moiety with (C₁-C₄)alkyl; or a pharmaceutically acceptable salt or ester thereof.

2. A compound of claim 1 wherein  represents a 6 membered ring containing 0 N atoms.
3. A compound of claim 2 wherein R¹ and R² are each independently selected from H, (C₁-C₃)alkoxy, F, and CF₃; R³ is selected from H, NH₂, and NHC(O)(C₁-C₃)alkyl; R⁴ is selected from H, halo, (C₁-C₃)alkoxy, CN, COR⁶, S(O)₂R⁷, N[(C₁-C₃)alkyl]₂, optionally substituted phenyl and optionally substituted (C₁-C₄)alkyl; and R⁵ is selected from H, (C₁-C₃)alkoxy, F and CN.
4. A compound of claim 3 wherein R⁵ is selected from H and F; and R⁴ is selected from H, halo, (C₁-C₃)alkoxy, CN, COR⁶, S(O)₂R⁷, N[(C₁-C₃)alkyl]₂, and optionally substituted (C₁-C₄)alkyl.
5. A compound of claim 4 wherein R¹ and R² are each H; R³ is NH₂; R⁴ is COR⁶, S(O)₂R⁷, and (C₁-C₄)alkyl optionally substituted with N[(C₁-C₃)alkyl]₂ and N[(C₃-C₆)cycloalkyl][(C₁-C₃)alkyl]; R⁵ is H; R⁶ is N[(C₁-C₃)alkyl]₂ and N[(C₃-C₆)cycloalkyl][(C₁-C₃)alkyl], R⁷ is N[(C₁-C₃)alkyl]₂; and R¹¹ and R¹² are each H.
6. A compound of claim 1 wherein  is 6 membered aromatic ring containing 1 or 2 N atoms.
7. A compound of claim 6 wherein R³ is selected from H, NH₂, and NHC(O)(C₁-C₃)alkyl; R⁴ is selected from H, halo, (C₁-C₃)alkoxy, CN, COR⁶, S(O)₂R⁷, N[(C₁-C₃)alkyl]₂, optionally substituted phenyl and optionally substituted (C₁-C₄)alkyl; and R⁵ is selected from H, (C₁-C₃)alkoxy, F and CN.
8. A method of treating a hyper-proliferative disorder comprising the administration to a mammal in need thereof of an effective amount of a compound of Formula I

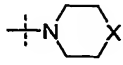
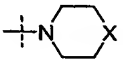
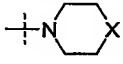
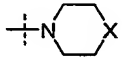




(I)

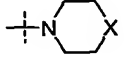
wherein



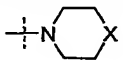
represents a 6 membered aromatic ring containing 0, 1 or 2 N atoms;

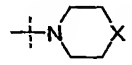
R^1 and R^2 are each independently selected from H, halo, CF_3 , $C(O)R^9$, ,
 (C₁-C₆)alkyl optionally substituted with up to two substituents selected from
 OH, (C₁-C₃)alkoxy, F, and phenyl,
 (C₁-C₆)alkoxy optionally substituted with one or two substituents each
 independently selected from  and
 $N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted
 up to two times with (C₁-C₃)alkoxy,
 $NH(C_1-C_3)alkyl$ where said alkyl is optionally substituted with up to two
 substituents each selected independently from OH, F, (C₁-C₃)alkoxy,
 $N[(C_1-C_3)alkyl]_2$, $NH(C_1-C_3)alkyl$, phenyl, pyrrolidinyl, and ,
 $N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted
 with up to two substituents each selected independently from OH, F,
 phenyl, and (C₁-C₃)alkoxy, said alkoxy being optionally
 substituted with ,
 pyrrolidinyl optionally substituted up to two times with $N[(C_1-C_3)alkyl]_2$,
 phenyl optionally substituted with up to two substituents each selected
 independently from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF_3 , and CN,
 with the proviso that when  contains 1 or 2 N atoms, R^1 and R^2 must each be
 H,
 and, R^1 and R^2 together with the adjacent C atoms to which they are attached
 form a ring selected from benzo, dioxolo and imidazo,
 said imidazo being optionally substituted up to two times with
 (C₁-C₃)alkyl,
 with the proviso that R^1 and R^2 together with the adjacent C atoms to
 which they are attached form a ring only when  contains no N atoms;
 R^3 is selected from H, (C₁-C₄)alkyl, OH, NO_2 , NH_2 , $NH(C_1-C_4)alkyl$, $NHC(O)(C_1-C_4)alkyl$
 and $NHC(O)phenyl$, said phenyl being optionally substituted with up to two
 substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo,
 CF_3 , and CN;

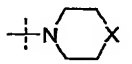
R^4 is selected from H, OH, halo, CN, $C(O)R^6$, $S(O)_2R^7$, $OSi[(C_1-C_4)alkyl]_3$, tetrazolyl, thienyl, pyrrolyl, pyrimidinyl, oxazolyl, furanyl, $(C_1-C_6)alkyl$, $(C_2-C_6)alkenyl$ or $(C_2-C_6)alkynyl$, each optionally substituted with OH, F, $OC(O)NHphenyl$, $NHC(O)(C_1-C_3)alkyl$, $C(O)NH_2$,

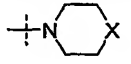
$C(O)NH(C_1-C_3)alkyl$, $C(O)N[(C_1-C_3)alkyl]_2$, , $(C_1-C_3)alkoxy$ optionally substituted up to two times with $(C_1-C_3)alkoxy$, $NHC(O)NH(C_1-C_3)alkyl$ where said alkyl is optionally substituted with up to two substituents independently selected from OH, $(C_1-C_3)alkoxy$, F and phenyl,

$NHC(O)NHphenyl$ where said phenyl is optionally substituted with up to two substituents independently selected from $(C_1-C_3)alkyl$,

$(C_1-C_3)alkoxy$, halo, CF_3 , CN, and , $NHC(O)N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted up to two times with $(C_1-C_3)alkoxy$, NH-phenyl, said phenyl being optionally substituted with up to two substituents independently selected from $(C_1-C_3)alkyl$,

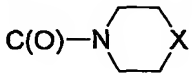
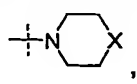
$(C_1-C_3)alkoxy$, halo, CN, and , $N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted up to two times with $(C_1-C_3)alkoxy$, phenyl optionally substituted with up to two substituents independently selected from $(C_1-C_3)alkyl$, $(C_1-C_3)alkoxy$, halo, CN, CF_3 , and

, pyrrolidinyl optionally substituted up to two times with $N[(C_1-C_3)alkyl]_2$, $(C_1-C_6)alkoxy$ optionally substituted with up to two substituents independently

selected from $(C_1-C_3)alkoxy$, pyrrolidinyl, , and $N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally substituted with up to two substituents independently selected from OH, F, $(C_1-C_3)alkoxy$ and phenyl,

$N[(C_1-C_4)alkyl]_2$ where each of said alkyl groups are independently optionally substituted with up to two substituents independently selected from OH, $(C_1-C_3)alkyl$, F, $(C_1-C_3)alkoxy$, and phenyl, oxadiazolyl optionally substituted up to two times with $(C_1-C_3)alkyl$,

phenyl optionally substituted with up to two substituents independently selected

from (C₁-C₃)alkoxy, CN, (C₁-C₃)alkyl, halo, , ,

C(O)(C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkoxy, OH, (C₁-C₃)alkoxy, F, and phenyl, and

C(O)N[(C₁-C₃)alkyl]₂ where each of said alkyl groups are independently optionally substituted up to two times with (C₁-C₃)alkoxy,

pyridyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl,

C(O)N[(C₁-C₃)alkyl]₂ where each of said alkyl groups are independently optionally substituted up to two times with (C₁-C₃)alkoxy, and

O-pyridyl optionally substituted with up to two substituents independently selected from CF₃, halo, and (C₁-C₃)alkyl;

R⁵ is selected from H, halo, CN, (C₁-C₆)alkoxy, and (C₁-C₆)alkyl;

R⁶ is selected from OH, NHR¹⁰, O-(C₃-C₆)cycloalkyl, (C₁-C₃)alkoxy, O-(C₂-C₆)alkenyl, O-(C₃-C₆)alkynyl,

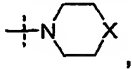
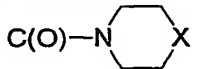
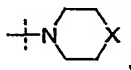
(C₁-C₆)alkyl optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

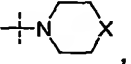
N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally substituted with up to two substituents independently selected from OH, CN, N[(C₁-C₄)alkyl]₂, (C₁-C₃)alkoxy, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl, and pyridyl,

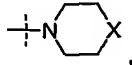
N[(C₁-C₃)alkyl]R⁸ where [(C₁-C₃)alkyl] is optionally substituted up to two times with (C₁-C₃)alkoxy,

N[(C₃-C₆)cycloalkyl](C₁-C₃)alkyl where said alkyl is substituted with up to two substituents independently selected from (C₁-C₃)alkoxy, OH, CN, N[(C₁-C₄)alkyl]₂, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₅-C₆)cycloalkyl, and pyridyl,


pyrrolidinyl optionally substituted with up to two substituents independently selected from NH₂, NH(C₁-C₃)alkyl, N[(C₁-C₄)alkyl]₂, C(O)NH₂, NHC(O)(C₁-C₃)alkyl, NHS(O)₂(C₁-C₃)alkyl, pyridyl, N[(C₁-C₃)alkyl]C(O)NH(C₁-C₃)alkyl, N[(C₁-C₃)alkyl]C(O)(C₁-C₃)alkyl, and (C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from N[(C₁-C₄)alkyl]₂, (C₁-C₃)alkoxy, and pyrrolidinyl,

morpholinyl optionally substituted up to two times with (C₁-C₃)alkyl,
 thiomorpholinyl optionally substituted up to two times with (C₁-C₃)alkyl,
 piperazinyl optionally substituted with up to two substituents independently
 selected from pyrazinyl, C(O)NH₂, C(O)NH-phenyl, C(O)-furanyl,
 C(O)(C₁-C₃)alkyl, C(O)NH(C₁-C₃)alkyl, C(O)N[(C₁-C₃)alkyl]R⁸,
 S(O)₂(C₁-C₃)alkyl, S(O)₂-phenyl, ,
 pyridyl optionally substituted with up to two substituents independently
 selected from (C₁-C₃)alkyl, CN and CF₃,
 phenyl optionally substituted with up to two substituents independently
 selected from (C₁-C₃)alkyl, CN, halo, CF₃, and (C₁-C₃)alkoxy,
 (C₁-C₃)alkyl optionally substituted with up to two substituents
 independently selected from OH, F, phenyl, (C₁-C₃)alkoxy,
 N[(C₁-C₃)alkyl]₂, pyrrolidinyl, C(O)-pyrrolidinyl, ,
, and
 pyridyl optionally substituted up to two times with (C₁-C₃)alkoxy,
 and
 piperidinyl optionally substituted with up to two substituents independently
 selected from phenyl, pyridyl, pyrrolidinyl and oxo-dihydrobenzimidazolyl;

R⁷ is selected from NH₂, pyrrolidinyl, ,
 NH(C₁-C₃)alkyl said alkyl being optionally substituted up to two times with
 (C₁-C₃)alkoxy,
 NH-phenyl said phenyl being optionally substituted with up to two substituents
 independently selected from (C₁-C₃)alkyl, CN, (C₁-C₄)alkoxy, halo and CF₃,
 N[(C₁-C₃)alkyl]₂ wherein each alkyl is independently optionally substituted up to
 two times with (C₁-C₄)alkoxy, and
 phenyl optionally substituted with up to two substituents independently selected
 from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃ and CN;
 R⁸ is selected from (C₁-C₃)alkoxy, pyridyl, piperidinyl, pyranal and
 phenyl, where each ring moiety is optionally substituted with up to two
 substituents independently selected from (C₁-C₃)alkoxy, and
 (C₁-C₃)alkyl;

R⁹ is selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, OH, ,

phenyl optionally substituted with (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN, N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally substituted with OH, CN, N[(C₁-C₄)alkyl]₂, (C₁-C₄)alkoxy, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl, and pyridyl, and pyrrolidinyl optionally substituted with N[(C₁-C₃)alkyl]₂,

and, only when  contains no N atoms, R⁹ is also selected from pyridyl, thienyl, and NHR¹⁰;

R¹⁰ is selected from H, indolyl,

(C₁-C₄)alkyl optionally substituted with up to two substituents independently selected from OH, F, phenyl, (C₁-C₄)alkoxy, NHC(O)(C₁-C₃)alkyl,

S-(C₁-C₃)alkyl, benzimidazolyl, indolyl, thienyl, pyrazolyl, ,

N[(C₁-C₄)alkyl]₂ where each alkyl is independently optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, CN, halo, CF₃, S(O)₂(C₁-C₃)alkyl, S(O)₂phenyl, and S(O)₂NH₂,

pyridyl optionally substituted up to two times with CF₃,

imidazolyl optionally substituted up to two times with (C₁-C₃)alkyl,

furyl optionally substituted up to two times with (C₁-C₄)alkyl, and

pyrrolidinyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (O), and

(C₁-C₄)alkyl optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

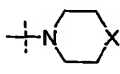
S(O)₂-phenyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (C₁-C₃)alkyl, halo, and CN,

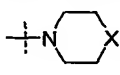
pyrazolyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl, and

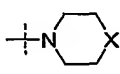
phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (C₁-C₄)alkyl, halo, CF₃, and CN,

benzothiazolyl optionally substituted up to two times with (C₁-C₄)alkyl,

thiazolyl, optionally substituted up to two times with (C₁-C₄)alkyl,
 thiadiazolyl, optionally substituted with up to two substituents independently
 selected from CF₃, (C₃-C₆)cycloalkyl, and (C₁-C₆)alkyl,
 phenyl optionally substituted with up to two substituents independently selected

from CN, halo, CF₃, N[(C₁-C₄)alkyl]₂, indolyl, ,
 O-pyridyl optionally substituted with C(O)NH(C₁-C₄)alkyl,
 (C₁-C₄)alkyl optionally substituted with up to two substituents

independently selected from pyridyl, , OH,
 (C₁-C₃)alkoxy, F, and phenyl, and
 (C₁-C₄)alkoxy optionally substituted with N[(C₁-C₄)alkyl]₂ where one
 alkyl group is optionally substituted with phenyl, or

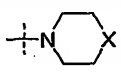
(C₁-C₄)alkoxy optionally substituted with ,
 pyridyl optionally substituted with phenoxy where said phenoxy is optionally
 substituted with up to two substituents independently selected
 from (C₁-C₄)alkyl and (C₁-C₄)alkoxy, and

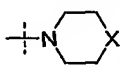
indazolyl optionally substituted up to two times with (C₁-C₄)alkyl;

R¹¹ and R¹² are each selected independently from H, F and Cl with the proviso that when
 one of R¹¹ and R¹² is F or Cl, the other must be H;

X is selected from O, S, CH₂, and NH, and

when X is NH, the H on NH is optionally replaced with pyridyl, pyrazinyl, phenyl,
 or (C₁-C₄)alkyl optionally substituted with up to two substituents
 independently selected from OH, (C₁-C₃)alkoxy, N[(C₁-C₃)alkyl]₂,
 C(O)-pyrrolidinyl, N[(C₁-C₄)alkyl]₂, and phenyl said phenyl being
 optionally substituted with up to two substituents
 independently selected from CN and (C₁-C₃)alkoxy,

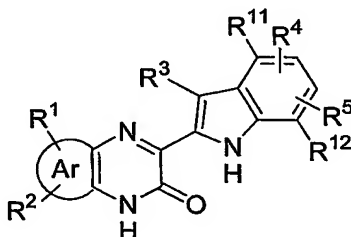
and when X is O, S, or CH₂, the  moiety is optionally substituted

by replacing any H atom in the  moiety with (C₁-C₄)alkyl;

or a pharmaceutically acceptable salt or ester thereof.

9. A method according to claim 8 wherein the hyperproliferative disorder is selected from breast cancer, lung cancer, colon cancer, pancreatic cancer, prostate cancer, skin cancer, leukemia, lymphoma, glioblastoma and head and neck cancers.

10. A method according to claim 9 wherein the hyperproliferative disorder is selected from breast cancer, lung cancer, colon cancer and pancreatic cancer.
11. A method of treating an angiogenic disorder comprising the administration to a mammal in need thereof of an effective amount of a compound of Formula I



(I)

wherein



represents a 6 membered aromatic ring containing 0, 1 or 2 N atoms;

R^1 and R^2 are each independently selected from H, halo, CF_3 , $C(O)R^9$, $\text{---}N\text{---}$ (where N is in a 6-membered ring with substituent X), (C_1-C_6) alkyl optionally substituted with up to two substituents selected from OH, (C_1-C_3) alkoxy, F, and phenyl,

(C_1-C_6) alkoxy optionally substituted with one or two substituents each

independently selected from $\text{---}N\text{---}$ (where N is in a 6-membered ring with substituent X) and

$N[(C_1-C_3)\text{alkyl}]_2$ where each alkyl is independently optionally substituted up to two times with (C_1-C_3) alkoxy,

$NH(C_1-C_3)\text{alkyl}$ where said alkyl is optionally substituted with up to two substituents each selected independently from OH, F, (C_1-C_3) alkoxy,

$N[(C_1-C_3)\text{alkyl}]_2$, $NH(C_1-C_3)\text{alkyl}$, phenyl, pyrrolidinyl, and $\text{---}N\text{---}$ (where N is in a 6-membered ring with substituent X),

$N[(C_1-C_3)\text{alkyl}]_2$ where each alkyl is independently optionally substituted with up to two substituents each selected independently from OH, F, phenyl, and (C_1-C_3) alkoxy, said alkoxy being optionally


substituted with $\text{---}N\text{---}$ (where N is in a 6-membered ring with substituent X),

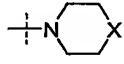
pyrrolidinyl optionally substituted up to two times with $N[(C_1-C_3)\text{alkyl}]_2$,

phenyl optionally substituted with up to two substituents each selected

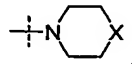
independently from (C_1-C_3) alkyl, (C_1-C_3) alkoxy, halo, CF_3 , and CN,

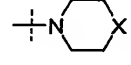
with the proviso that when Ar contains 1 or 2 N atoms, R^1 and R^2 must each be H,

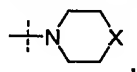
and, R¹ and R² together with the adjacent C atoms to which they are attached form a ring selected from benzo, dioxolo and imidazo, said imidazo being optionally substituted up to two times with (C₁-C₃)alkyl, with the proviso that R¹ and R² together with the adjacent C atoms to which they are attached form a ring only when  contains no N atoms; R³ is selected from H, (C₁-C₄)alkyl, OH, NO₂, NH₂, NH(C₁-C₄)alkyl, NHC(O)(C₁-C₄)alkyl and NHC(O)phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN; R⁴ is selected from H, OH, halo, CN, C(O)R⁶, S(O)₂R⁷, OSi[(C₁-C₄)alkyl]₃, tetrazolyl, thienyl, pyrrolyl, pyrimidinyl, oxazolyl, furanyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl or (C₂-C₆)alkynyl, each optionally substituted with OH, F, OC(O)NHphenyl, NHC(O)(C₁-C₃)alkyl, C(O)NH₂,

C(O)NH(C₁-C₃)alkyl, C(O)N[(C₁-C₃)alkyl]₂, , (C₁-C₃)alkoxy optionally substituted up to two times with (C₁-C₃)alkoxy, NHC(O)NH(C₁-C₃)alkyl where said alkyl is optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F and phenyl,

NHC(O)NHphenyl where said phenyl is optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl,

(C₁-C₃)alkoxy, halo, CF₃, CN, and , NHC(O)N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally substituted up to two times with (C₁-C₃)alkoxy, NH-phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl,

(C₁-C₃)alkoxy, halo, CN, and , N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally substituted up to two times with (C₁-C₃)alkoxy, phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CN, CF₃, and



pyrrolidinyl optionally substituted up to two times with $N[(C_1-C_3)alkyl]_2$,
 $(C_1-C_6)alkoxy$ optionally substituted with up to two substituents independently

selected from $(C_1-C_3)alkoxy$, pyrrolidinyl, ,

and $N[(C_1-C_3)alkyl]_2$ where each alkyl is independently optionally
 substituted with up to two substituents independently selected from
 OH, F, $(C_1-C_3)alkoxy$ and phenyl,

$N[(C_1-C_4)alkyl]_2$ where each of said alkyl groups are independently optionally
 substituted with up to two substituents independently selected from OH,
 $(C_1-C_3)alkyl$, F, $(C_1-C_3)alkoxy$, and phenyl,

oxadiazolyl optionally substituted up to two times with $(C_1-C_3)alkyl$,
 phenyl optionally substituted with up to two substituents independently selected

from $(C_1-C_3)alkoxy$, CN, $(C_1-C_3)alkyl$, halo, , ,

$C(O)(C_1-C_3)alkyl$ optionally substituted with up to two substituents
 independently selected from $(C_1-C_3)alkoxy$, OH, $(C_1-C_3)alkoxy$,
 F, and phenyl, and

$C(O)N[(C_1-C_3)alkyl]_2$ where each of said alkyl groups are independently
 optionally substituted up to two times with $(C_1-C_3)alkoxy$,

pyridyl optionally substituted with up to two substituents independently selected
 from $(C_1-C_3)alkyl$,

$C(O)N[(C_1-C_3)alkyl]_2$ where each of said alkyl groups are independently optionally
 substituted up to two times with $(C_1-C_3)alkoxy$, and

O-pyridyl optionally substituted with up to two substituents independently selected
 from CF_3 , halo, and $(C_1-C_3)alkyl$;

R^5 is selected from H, halo, CN, $(C_1-C_6)alkoxy$, and $(C_1-C_6)alkyl$;

R^6 is selected from OH, NHR^{10} , O- $(C_3-C_6)cycloalkyl$, $(C_1-C_3)alkoxy$, O- $(C_2-C_6)alkenyl$,
 O- $(C_3-C_6)alkynyl$,

$(C_1-C_6)alkyl$ optionally substituted with up to two substituents independently
 selected from OH, $(C_1-C_3)alkoxy$, F, and phenyl,

$N[(C_1-C_4)alkyl]_2$ where each of said alkyl groups are independently optionally
 substituted with up to two substituents independently selected from OH,
 CN, $N[(C_1-C_4)alkyl]_2$, $(C_1-C_3)alkoxy$, $S(O)_2$ -phenyl, $S(O)_2(C_1-C_3)alkyl$,
 phenyl, furyl, tetrahydrofuryl, $(C_3-C_6)cycloalkyl$, and pyridyl,

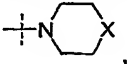
$N[(C_1-C_3)alkyl]R^8$ where $[(C_1-C_3)alkyl]$ is optionally substituted up to two times with
 $(C_1-C_3)alkoxy$,

$N[(C_3-C_6)\text{cycloalkyl}](C_1-C_3)\text{alkyl}$ where said alkyl is substituted with up to two substituents independently selected from $(C_1-C_3)\text{alkoxy}$, OH, CN, $N[(C_1-C_4)\text{alkyl}]_2$, $S(O)_2\text{-phenyl}$, $S(O)_2(C_1-C_3)\text{alkyl}$, phenyl, furyl, tetrahydrofuryl, $(C_5-C_6)\text{cycloalkyl}$, and pyridyl,

pyrrolidinyl optionally substituted with up to two substituents independently selected from NH_2 , $NH(C_1-C_3)\text{alkyl}$, $N[(C_1-C_4)\text{alkyl}]_2$, $C(O)NH_2$, $NHC(O)(C_1-C_3)\text{alkyl}$, $NHS(O)_2(C_1-C_3)\text{alkyl}$, pyridyl, $N[(C_1-C_3)\text{alkyl}]C(O)NH(C_1-C_3)\text{alkyl}$, $N[(C_1-C_3)\text{alkyl}]C(O)(C_1-C_3)\text{alkyl}$, and $(C_1-C_3)\text{alkyl}$ optionally substituted with up to two substituents independently selected from $N[(C_1-C_4)\text{alkyl}]_2$, $(C_1-C_3)\text{alkoxy}$, and pyrrolidinyl,

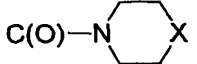
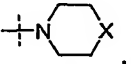
morpholinyl optionally substituted up to two times with $(C_1-C_3)\text{alkyl}$,

thiomorpholinyl optionally substituted up to two times with $(C_1-C_3)\text{alkyl}$,

piperazinyl optionally substituted with up to two substituents independently selected from pyrazinyl, $C(O)NH_2$, $C(O)NH\text{-phenyl}$, $C(O)\text{-furyl}$, $C(O)(C_1-C_3)\text{alkyl}$, $C(O)NH(C_1-C_3)\text{alkyl}$, $C(O)N[(C_1-C_3)\text{alkyl}]R^8$, $S(O)_2(C_1-C_3)\text{alkyl}$, $S(O)_2\text{-phenyl}$, ,

pyridyl optionally substituted with up to two substituents independently selected from $(C_1-C_3)\text{alkyl}$, CN and CF_3 ,

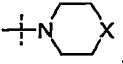
phenyl optionally substituted with up to two substituents independently selected from $(C_1-C_3)\text{alkyl}$, CN, halo, CF_3 , and $(C_1-C_3)\text{alkoxy}$,

$(C_1-C_3)\text{alkyl}$ optionally substituted with up to two substituents independently selected from OH, F, phenyl, $(C_1-C_3)\text{alkoxy}$, $N[(C_1-C_3)\text{alkyl}]_2$, pyrrolidinyl, $C(O)\text{-pyrrolidinyl}$, , , and

pyridyl optionally substituted up to two times with $(C_1-C_3)\text{alkoxy}$,

and

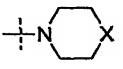
piperidinyl optionally substituted with up to two substituents independently selected from phenyl, pyridyl, pyrrolidinyl and oxo-dihydrobenzimidazolyl;


R^7 is selected from NH_2 , pyrrolidinyl, ,

$NH(C_1-C_3)\text{alkyl}$ said alkyl being optionally substituted up to two times with $(C_1-C_3)\text{alkoxy}$,

$NH\text{-phenyl}$ said phenyl being optionally substituted with up to two substituents

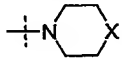
independently selected from (C₁-C₃)alkyl, CN, (C₁-C₄)alkoxy, halo and CF₃, N[(C₁-C₃)alkyl]₂ wherein each alkyl is independently optionally substituted up to two times with (C₁-C₄)alkoxy, and phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃ and CN; R⁸ is selected from (C₁-C₃)alkoxy, pyridyl, piperidiny, pyranly and phenyl, where each ring moiety is optionally substituted with up to two substituents independently selected from (C₁-C₃)alkoxy, and (C₁-C₃)alkyl;

R⁹ is selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, OH, , phenyl optionally substituted with (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN, N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally substituted with OH, CN, N[(C₁-C₄)alkyl]₂, (C₁-C₄)alkoxy, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl, and pyridyl, and pyrrolidiny optionally substituted with N[(C₁-C₃)alkyl]₂,

and, only when  contains no N atoms, R⁹ is also selected from pyridyl, thienyl, and NHR¹⁰;

R¹⁰ is selected from H, indolyl,

(C₁-C₄)alkyl optionally substituted with up to two substituents independently selected from OH, F, phenyl, (C₁-C₄)alkoxy, NHC(O)(C₁-C₃)alkyl,

S-(C₁-C₃)alkyl, benzimidazolyl, indolyl, thienyl, pyrazolyl, , N[(C₁-C₄)alkyl]₂ where each alkyl is independently optionally

substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, CN, halo, CF₃, S(O)₂(C₁-C₃)alkyl, S(O)₂phenyl, and S(O)₂NH₂,

pyridyl optionally substituted up to two times with CF₃,

imidazolyl optionally substituted up to two times with (C₁-C₃)alkyl,

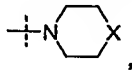
furyl optionally substituted up to two times with (C₁-C₄)alkyl, and

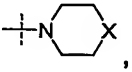
pyrrolidiny optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (O), and

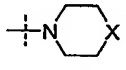
(C₁-C₄)alkyl optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

S(O)₂-phenyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (C₁-C₃)alkyl, halo, and CN, pyrazolyl optionally substituted with up to two substituents independently selected from (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl, and phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₄)alkoxy, (C₁-C₄)alkyl, halo, CF₃, and CN,

benzothiazolyl optionally substituted up to two times with (C₁-C₄)alkyl, thiazolyl, optionally substituted up to two times with (C₁-C₄)alkyl, thiadiazolyl, optionally substituted with up to two substituents independently selected from CF₃, (C₃-C₆)cycloalkyl, and (C₁-C₆)alkyl, phenyl optionally substituted with up to two substituents independently selected

from CN, halo, CF₃, N[(C₁-C₄)alkyl]₂, indolyl, , O-pyridyl optionally substituted with C(O)NH(C₁-C₄)alkyl, (C₁-C₄)alkyl optionally substituted with up to two substituents

independently selected from pyridyl, , OH, (C₁-C₃)alkoxy, F, and phenyl, and (C₁-C₄)alkoxy optionally substituted with N[(C₁-C₄)alkyl]₂ where one alkyl group is optionally substituted with phenyl, or

(C₁-C₄)alkoxy optionally substituted with ,

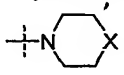
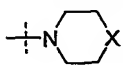
pyridyl optionally substituted with phenoxy where said phenoxy is optionally substituted with up to two substituents independently selected from (C₁-C₄)alkyl and (C₁-C₄)alkoxy, and

indazolyl optionally substituted up to two times with (C₁-C₄)alkyl;

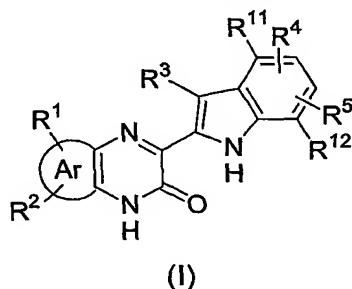
R¹¹ and R¹² are each selected independently from H, F and Cl with the proviso that when one of R¹¹ and R¹² is F or Cl, the other must be H;

X is selected from O, S, CH₂, and NH, and

when X is NH, the H on NH is optionally replaced with pyridyl, pyrazinyl, phenyl, or (C₁-C₄)alkyl optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, N[(C₁-C₃)alkyl]₂, C(O)-pyrrolidinyl, N[(C₁-C₄)alkyl]₂, and phenyl said phenyl being

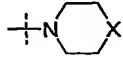
optionally substituted with up to two substituents
independently selected from CN and (C₁-C₃)alkoxy,
and when X is O, S, or CH₂, the  moiety is optionally substituted
by replacing any H atom in the  moiety with (C₁-C₄)alkyl;
or a pharmaceutically acceptable salt or ester thereof.

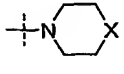
12. A method of claim 11 where the angiogenic disorder is selected from diabetic retinopathy, macular degeneration, angiofibromas, a rheumatic inflammatory disease, a neoplastic disease, and a solid tumor growth.
13. A method of claim 12 where the angiogenic disorder is selected from breast cancer, lung cancer, colon cancer, prostate cancer and pancreatic cancer.
14. A pharmaceutical composition comprising a compound of Formula I



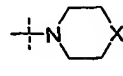
wherein

 represents a 6 membered aromatic ring containing 0, 1 or 2 N atoms;

R¹ and R² are each independently selected from H, halo, CF₃, C(O)R⁹, ,
(C₁-C₆)alkyl optionally substituted with up to two substituents selected from
OH, (C₁-C₃)alkoxy, F, and phenyl,
(C₁-C₆)alkoxy optionally substituted with one or two substituents each

independently selected from  and
N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally substituted
up to two times with (C₁-C₃)alkoxy,

NH(C₁-C₃)alkyl where said alkyl is optionally substituted with up to two
substitutents each selected independently from OH, F, (C₁-C₃)alkoxy,

N[(C₁-C₃)alkyl]₂, NH(C₁-C₃)alkyl, phenyl, pyrrolidinyl, and ,
N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally substituted


with up to two substituents each selected independently from OH, F, phenyl, and (C₁-C₃)alkoxy, said alkoxy being optionally

substituted with ,

pyrrolidinyl optionally substituted up to two times with N[(C₁-C₃)alkyl]₂,

phenyl optionally substituted with up to two substituents each selected

independently from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN,

with the proviso that when  contains 1 or 2 N atoms, R¹ and R² must each be H,

and, R¹ and R² together with the adjacent C atoms to which they are attached form a ring selected from benzo, dioxolo and imidazo,

said imidazo being optionally substituted up to two times with (C₁-C₃)alkyl,

with the proviso that R¹ and R² together with the adjacent C atoms to

which they are attached form a ring only when  contains no N atoms;

R³ is selected from H, (C₁-C₄)alkyl, OH, NO₂, NH₂, NH(C₁-C₄)alkyl, NHC(O)(C₁-C₄)alkyl and NHC(O)phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN;

R⁴ is selected from H, OH, halo, CN, C(O)R⁶, S(O)₂R⁷, OSi[(C₁-C₄)alkyl]₃, tetrazolyl, thienyl, pyrrolyl, pyrimidinyl, oxazolyl, furanyl,

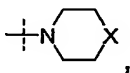
(C₁-C₆)alkyl, (C₂-C₆)alkenyl or (C₂-C₆)alkynyl, each optionally substituted with OH, F, OC(O)NHphenyl, NHC(O)(C₁-C₃)alkyl, C(O)NH₂,

C(O)NH(C₁-C₃)alkyl, C(O)N[(C₁-C₃)alkyl]₂, ,

(C₁-C₃)alkoxy optionally substituted up to two times with (C₁-C₃)alkoxy, NHC(O)NH(C₁-C₃)alkyl where said alkyl is optionally substituted

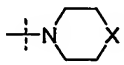
with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F and phenyl,

NHC(O)NHphenyl where said phenyl is optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl,

(C₁-C₃)alkoxy, halo, CF₃, CN, and ,

NHC(O)N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally substituted up to two times with (C₁-C₃)alkoxy,

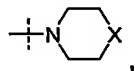
NH-phenyl, said phenyl being optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl,

(C₁-C₃)alkoxy, halo, CN, and ,

N[(C₁-C₃)alkyl]₂ where each alkyl is independently

optionally substituted up to two times with (C₁-C₃)alkoxy,

phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CN, CF₃, and



pyrrolidinyl optionally substituted up to two times with N[(C₁-C₃)alkyl]₂,

(C₁-C₆)alkoxy optionally substituted with up to two substituents independently

selected from (C₁-C₃)alkoxy, pyrrolidinyl, ,

and N[(C₁-C₃)alkyl]₂ where each alkyl is independently optionally

substituted with up to two substituents independently selected from OH, F, (C₁-C₃)alkoxy and phenyl,

N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkyl, F, (C₁-C₃)alkoxy, and phenyl,

oxadiazolyl optionally substituted up to two times with (C₁-C₃)alkyl,

phenyl optionally substituted with up to two substituents independently selected

from (C₁-C₃)alkoxy, CN, (C₁-C₃)alkyl, halo, , ,

C(O)(C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkoxy, OH, (C₁-C₃)alkoxy, F, and phenyl, and

C(O)N[(C₁-C₃)alkyl]₂ where each of said alkyl groups are independently optionally substituted up to two times with (C₁-C₃)alkoxy,

pyridyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl,

C(O)N[(C₁-C₃)alkyl]₂ where each of said alkyl groups are independently optionally substituted up to two times with (C₁-C₃)alkoxy, and

O-pyridyl optionally substituted with up to two substituents independently selected from CF₃, halo, and (C₁-C₃)alkyl;

R⁵ is selected from H, halo, CN, (C₁-C₆)alkoxy, and (C₁-C₆)alkyl;

R⁶ is selected from OH, NHR¹⁰, O-(C₃-C₆)cycloalkyl, (C₁-C₃)alkoxy, O-(C₂-C₆)alkenyl,

O-(C₃-C₆)alkynyl,

(C₁-C₆)alkyl optionally substituted with up to two substituents independently selected from OH, (C₁-C₃)alkoxy, F, and phenyl,

N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally substituted with up to two substituents independently selected from OH, CN, N[(C₁-C₄)alkyl]₂, (C₁-C₃)alkoxy, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl, and pyridyl,

N[(C₁-C₃)alkyl]R⁸ where [(C₁-C₃)alkyl] is optionally substituted up to two times with (C₁-C₃)alkoxy,

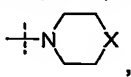
N[(C₃-C₆)cycloalkyl](C₁-C₃)alkyl where said alkyl is substituted with up to two substituents independently selected from (C₁-C₃)alkoxy, OH, CN, N[(C₁-C₄)alkyl]₂, S(O)₂-phenyl, S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₅-C₆)cycloalkyl, and pyridyl,

pyrrolidinyl optionally substituted with up to two substituents independently selected from NH₂, NH(C₁-C₃)alkyl, N[(C₁-C₄)alkyl]₂, C(O)NH₂, NHC(O)(C₁-C₃)alkyl, NHS(O)₂(C₁-C₃)alkyl, pyridyl, N[(C₁-C₃)alkyl]C(O)NH(C₁-C₃)alkyl, N[(C₁-C₃)alkyl]C(O)(C₁-C₃)alkyl, and (C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from N[(C₁-C₄)alkyl]₂, (C₁-C₃)alkoxy, and pyrrolidinyl,

morpholinyl optionally substituted up to two times with (C₁-C₃)alkyl,

thiomorpholinyl optionally substituted up to two times with (C₁-C₃)alkyl,

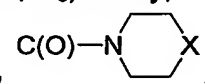
piperazinyl optionally substituted with up to two substituents independently selected from pyrazinyl, C(O)NH₂, C(O)NH-phenyl, C(O)-furyl, C(O)(C₁-C₃)alkyl, C(O)NH(C₁-C₃)alkyl, C(O)N[(C₁-C₃)alkyl]R⁸,

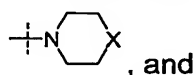
S(O)₂(C₁-C₃)alkyl, S(O)₂-phenyl, ,

pyridyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, CN and CF₃,

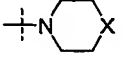
phenyl optionally substituted with up to two substituents independently selected from (C₁-C₃)alkyl, CN, halo, CF₃, and (C₁-C₃)alkoxy,

(C₁-C₃)alkyl optionally substituted with up to two substituents independently selected from OH, F, phenyl, (C₁-C₃)alkoxy,

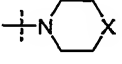
N[(C₁-C₃)alkyl]₂, pyrrolidinyl, C(O)-pyrrolidinyl, ,


, and

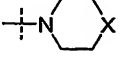
pyridyl optionally substituted up to two times with (C₁-C₃)alkoxy,
 and
 piperidinyl optionally substituted with up to two substituents independently
 selected from phenyl, pyridyl, pyrrolidinyl and oxo-dihydrobenzimidazolyl;

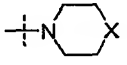
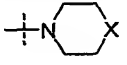
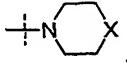
R⁷ is selected from NH₂, pyrrolidinyl, ,
 NH(C₁-C₃)alkyl said alkyl being optionally substituted up to two times with
 (C₁-C₃)alkoxy,
 NH-phenyl said phenyl being optionally substituted with up to two substituents
 independently selected from (C₁-C₃)alkyl, CN, (C₁-C₄)alkoxy, halo and CF₃,
 N[(C₁-C₃)alkyl]₂ wherein each alkyl is independently optionally substituted up to
 two times with (C₁-C₄)alkoxy, and
 phenyl optionally substituted with up to two substituents independently selected
 from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃ and CN;

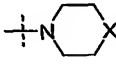
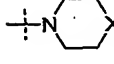
R⁸ is selected from (C₁-C₃)alkoxy, pyridyl, piperidinyl, pyranyl and
 phenyl, where each ring moiety is optionally substituted with up to two
 substituents independently selected from (C₁-C₃)alkoxy, and
 (C₁-C₃)alkyl;

R⁹ is selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, OH, ,
 phenyl optionally substituted with (C₁-C₃)alkyl, (C₁-C₃)alkoxy, halo, CF₃, and CN,
 N[(C₁-C₄)alkyl]₂ where each of said alkyl groups are independently optionally
 substituted with OH, CN, N[(C₁-C₄)alkyl]₂, (C₁-C₄)alkoxy, S(O)₂-phenyl,
 S(O)₂(C₁-C₃)alkyl, phenyl, furyl, tetrahydrofuryl, (C₃-C₆)cycloalkyl,
 and pyridyl, and
 pyrrolidinyl optionally substituted with N[(C₁-C₃)alkyl]₂.

and, only when  contains no N atoms, R⁹ is also selected from pyridyl,
 thienyl, and NHR¹⁰;

R¹⁰ is selected from H, indolyl,
 (C₁-C₄)alkyl optionally substituted with up to two substituents independently
 selected from OH, F, phenyl, (C₁-C₄)alkoxy, NHC(O)(C₁-C₃)alkyl,
 S-(C₁-C₃)alkyl, benzimidazolyl, indolyl, thienyl, pyrazolyl, ,
 N[(C₁-C₄)alkyl]₂ where each alkyl is independently optionally
 substituted with up to two substituents independently selected from

OH, (C₁-C₃)alkoxy, F, and phenyl,
 phenyl optionally substituted with up to two substituents independently
 selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, CN, halo,
 CF₃, S(O)₂(C₁-C₃)alkyl, S(O)₂phenyl, and S(O)₂NH₂,
 pyridyl optionally substituted up to two times with CF₃,
 imidazolyl optionally substituted up to two times with (C₁-C₃)alkyl,
 furyl optionally substituted up to two times with (C₁-C₄)alkyl, and
 pyrrolidinyl optionally substituted with up to two substituents independently
 selected from (C₁-C₄)alkoxy, (O), and
 (C₁-C₄)alkyl optionally substituted with up to two substituents
 independently selected from OH, (C₁-C₃)alkoxy, F,
 and phenyl,
 S(O)₂-phenyl optionally substituted with up to two substituents independently
 selected from (C₁-C₄)alkoxy, (C₁-C₃)alkyl, halo, and CN,
 pyrazolyl optionally substituted with up to two substituents independently selected
 from (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl, and
 phenyl, said phenyl being optionally substituted with up to two substituents
 independently selected from (C₁-C₄)alkoxy, (C₁-C₄)alkyl, halo, CF₃,
 and CN,
 benzothiazolyl optionally substituted up to two times with (C₁-C₄)alkyl,
 thiazolyl, optionally substituted up to two times with (C₁-C₄)alkyl,
 thiadiazolyl, optionally substituted with up to two substituents independently
 selected from CF₃, (C₃-C₆)cycloalkyl, and (C₁-C₆)alkyl,
 phenyl optionally substituted with up to two substituents independently selected
 from CN, halo, CF₃, N[(C₁-C₄)alkyl]₂, indolyl, ,
 O-pyridyl optionally substituted with C(O)NH(C₁-C₄)alkyl,
 (C₁-C₄)alkyl optionally substituted with up to two substituents
 independently selected from pyridyl, , OH,
 (C₁-C₃)alkoxy, F, and phenyl, and
 (C₁-C₄)alkoxy optionally substituted with N[(C₁-C₄)alkyl]₂ where one
 alkyl group is optionally substituted with phenyl, or
 (C₁-C₄)alkoxy optionally substituted with ,
 pyridyl optionally substituted with phenoxy where said phenoxy is optionally
 substituted with up to two substituents independently selected

from (C₁-C₄)alkyl and (C₁-C₄)alkoxy, and
indazolyl optionally substituted up to two times with (C₁-C₄)alkyl;
R¹¹ and R¹² are each selected independently from H, F and Cl with the proviso that when
one of R¹¹ and R¹² is F or Cl, the other must be H;
X is selected from O, S, CH₂, and NH, and
when X is NH, the H on NH is optionally replaced with pyridyl, pyrazinyl, phenyl,
or (C₁-C₄)alkyl optionally substituted with up to two substituents
independently selected from OH, (C₁-C₃)alkoxy, N[(C₁-C₃)alkyl]₂,
C(O)-pyrrolidinyl, N[(C₁-C₄)alkyl]₂, and phenyl said phenyl being
optionally substituted with up to two substituents
independently selected from CN and (C₁-C₃)alkoxy,
and when X is O, S, or CH₂, the  moiety is optionally substituted
by replacing any H atom in the  moiety with (C₁-C₄)alkyl;
or a pharmaceutically acceptable salt or ester thereof.